Edition: BP 2025 (Ph. Eur. 11.6 update)

Salbutamol Tablets

General Notices

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Salbutamol Tablets contain Salbutamol Sulfate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of salbutamol, $C_{13}H_{21}NO_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

B. Shake a quantity of the powdered tablets containing the equivalent of 4 mg of salbutamol with 10 mL of *water* and filter. The filtrate yields the reactions characteristic of *sulfates*, Appendix VI.

TESTS

Dissolution

Carry out the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 500 mL of 0.01M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) After 45 minutes withdraw a sample of the medium and filter (a 0.45-µm cellulose acetate filter is suitable). Dilute with the dissolution medium, if necessary, to produce a solution expected to contain the equivalent of 0.0004% w/v of salbutamol.
(2) 0.00048% w/v of *salbutamol sulfate BPCRS* in *water*.
(3) 0.04% w/v of *2-tert-butylamino-1-(4-hydroxy-3-methylphenyl)ethanol BPCRS* (impurity C) and 0.048% w/v of *salbutamol sulfate BPCRS* in *methanol* (*10%*).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 276 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

5 volumes of *propan-2-ol*, 30 volumes of 0.05M *ammonium acetate* and 65 volumes of *water*, adjusted to pH 4.5 with *glacial acetic acid*.

When the chromatograms are recorded under the prescribed conditions, the retention time of salbutamol is about 2 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to salbutamol and impurity C is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of salbutamol, $C_{13}H_{21}NO_3$, in the medium from the chromatograms obtained and using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*.

LIMITS

The amount of salbutamol released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Disperse a quantity of the powdered tablets in sufficient mobile phase to produce a solution containing the equivalent of 0.02% w/v of salbutamol and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes and further dilute 1 volumes of this solution to 5 volumes.
(3) 0.02% w/v of *salbutamol for peak identification EPCRS*.
(4) 0.02% w/v of *salbutamol impurity standard BPCRS*.
(5) 0.00004% w/v of each of *salbutamol sulfate BPCRS* and *salbutamol impurity B BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.9 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Symmetry C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 25 times the retention time of salbutamol.

MOBILE PHASE

22 volumes of *acetonitrile R1* and 78 volumes of a solution containing 0.287% w/v of *sodium heptanesulfonate* and 0.25% w/v of *potassium dihydrogen orthophosphate* adjusted to pH 3.7 with 2M *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution* between the peaks due to salbutamol and impurity B is at least 3.0.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of salbutamol in solution (2).

For the reporting threshold, use the concentration of salbutamol in solution (2).

For peak identification, use solutions (3) and (4).

Salbutamol retention time: about 3 minutes.

Relative retention: impurity B, about 1.4; impurity D, about 2.7; impurity F, about 6.3.

Correction factors: impurity D, multiply by 0.5.

LIMITS

— impurity F: not more than 0.8%;

— impurity D: not more than 0.6%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 2.0%;

— reporting threshold: 0.1%.

Uniformity of content

Tablets containing less than the equivalent of 2 mg and/or less than 2% w/w of salbutamol comply with the requirements stated under Tablets using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Add 50 mL of 0.05M *hydrochloric acid* to one tablet, shake for 1 hour, add sufficient 0.05M *hydrochloric acid* to produce 100 mL, mix, centrifuge and use the supernatant liquid.
(2) 0.0024% w/v of *salbutamol sulfate BPCRS* in *water*.
(3) 0.05% w/v of *2-tert-butylamino-1-(4-hydroxy-3-methylphenyl)ethanol BPCRS* (impurity C) and 0.06% w/v of *salbutamol sulfate BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to salbutamol and impurity C is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{13}H_{21}NO_3$ in each tablet using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*.

ASSAY

For tablets containing the equivalent of less than 2 mg and/or less than 2% w/w of salbutamol

Use the average of the individual results determined in the test for Uniformity of content.

For tablets containing the equivalent of 2 mg or more and 2% w/w or more of salbutamol

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake 10 tablets with 100 mL of *water* for 1 hour, add sufficient *water* to produce a solution containing the equivalent of 0.04% w/v of salbutamol, mix, centrifuge and use the supernatant liquid.
(2) 0.048% w/v of *salbutamol sulfate BPCRS* in *water*.
(3) 0.04% w/v of *2-tert-butylamino-1-(4-hydroxy-3-methylphenyl)ethanol BPCRS* (impurity C) and 0.048% w/v of *salbutamol sulfate BPCRS* in *methanol* (*10%*).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to salbutamol and impurity C is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of salbutamol, $C_{13}H_{21}NO_3$, in the tablets from the chromatograms obtained and using the declared content of $C_{13}H_{21}NO_3$ in *salbutamol sulfate BPCRS*.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of salbutamol.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C, D, E, F, G, H, I, J and P listed under Salbutamol Sulfate.